REMARKS

Reconsideration is requested.

Claims 29-35 and 37 have been canceled above, without prejudice. Claims 40-50 have been added. The revised claims find support throughout the specification. No new matter has been added. Claims 22-28, 38 and 40-50 are pending.

The claims define methods of inhibiting angiogenesis and treatment of mucosal tunours. The claims further refer to a "cofactor which stabilises the complex in a biologically active form, wherein the cofactor is a cis C18:1:9 or C18:1:11 fatty acid or a different fatty acid with a similar configuration" which is described on page 11, lines 15-16 and lines 20-21. Alpha-lactalbumin from human and bovine as well as different groups and subgroups of fatty acids, as described in the specification such as on page 9, line 32.

The specification has been revised in response to the Examiner's objections to same. Withdrawal of the objections to the specification in view of the above amendments is requested.

The obviousness type double patenting rejection of claims 22, 29, 37 and 28 over claims 1-16 of U.S. Patent No. 7,270,822 B2 is obviated by the above amendments.

The methods of the pending claims would not have been obvious in view of the claims of the cited patent. Withdrawal of the double patenting rejection is requested.

To the extent not obviated by the above amendments, the Section 112, first paragraph "enablement", rejection of claims 22-35, 37 and 38 is traversed.

Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments. To the extent not obviated by the above amendments, the Section 112, first paragraph "written description", rejection of claims 22-35, 37 and 38 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following further comments.

The applicant submits that one of ordinary skill in the art will be able to make and use the claimed invention without undue experimentation and that one of ordinary skill in the art will appreciate that the applicants were in possession of the claimed invention at the time the application was filed.

The Examiner will appreciate that a patent application need not, and often preferably does not, include a description of what is known to one of ordinary skill in the art. A patent specification is directed to one of ordinary skill in the art.

The ordinarily skilled person knows that alpha-lactalbumin sequences from multiple species are highly homologues. The Acharya KR, 1991 reference cited in the present application, for example, teaches that the amino acid sequences from human, bovine, sheep and goat are approximately 75 % identical, and that multiple domains including the Ca^{2+} binding region are highly conserved. An alignment of alpha-lactalbumin from multiple species is found in Watanabe, M et al 2000, J. Vet. Med. Sci. 62(11):1217-1219. The applicant believes that a person of ordinary skill in the art will appreciate from such an alignment, for example, the amino acid residues which may be mutated. Residues not marked are highly flexible as the species comprise amino acids with different chemical properties in these positions. Positions marked with "." or ":" are indicative for a position which tolerate at least conservative modifications. An asterisk

indicates conserved residues, which are preferably not modified unless otherwise specified. Based at least on an alignment of alpha-lactalbumin from different species a person of ordinary skill in the art would be able to reasonably predict suitable variants comprising one or more amino acid substitutions without interfering with the function of the protein. In the particular situation wherein mutations in specific regions are desired, such as for disruption of the Ca^{2+} binding region, mutations of conserved residues may be preferred.

A person of ordinary skill in the art is able to reasonably predict suitable variants of human or bovine alpha-lactalbumin that may be used according to the invention. The ordinarily skilled person will appreciate that the applicants were therefore in possession of the claimed invention and that the claimed invention could be made without undue experimentation.

Based on knowledge from Svensson et al 2000, cited in the application (page 10 line 8), for example, such variants are readily purified from E.coli. Therefore generation of alpha-lactalbumin variants or fragments requires only routine experimentation.

The applicant further notes that the specification describes that other reagents are useful in the conversion of human a-lactalbumin to HAMLET. For example, on page 10, lines 6-10 that "In particular, it has been reported previously that oleic acid (C18:1:9cis) is required for HAMLET production (M. Svensson, et al., (2000) Proc Natl Acad Sci USA, 97, 4221-6). More recently, it has been found that other fatty acids may act as co-factors in a similar way. For example PCT/IB03/01293, to which a reference is provided in the present specification, discloses that unsaturated fatty acids different from oleic acid can participate in forming a biologically active complex. The description

discloses the activity of a several C16-C18 unsaturated fatty acids. Evaluation of suitable cofactors capable of stabilising the complex in a biologically active form according to the present disclosure may be performed by the ordinarily skilled person using the method described by Swenson et al. 2000 provided as a reference in the application. Thus based on the present application in combination with PCT/IB03/01293 and Swenson et al. 2000, for example, the applicant believes that the ordinarily skilled person is able to make and use the claimed invention without undue experimentation, such as by determining the biological activity of alpha-lactalbumin in complexes with an unsaturated fatty acids. The applicant submits that undue experimentation is not required to make and use cofactors according to the claimed invention. The applicant further submits that PCT/IB03/01293 and the present specification describe that several fatty acids are useful in the conversion of human a-lactalbumin to HAMLET.

Withdrawal of the Section 112, first paragraph, rejections are requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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